PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/007131	30.06.2004	01.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/50, A61K31/00

Applicant
KRKA, TOVARNA ZDRAVIL, D.D. NOVO MESTO

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Luangkhot, N

Telephone No. +49 89 2399-7857

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/007131

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-27
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/EP2004/007131

Re Item I
Basis of the report

1) The formulations in claims 22-25 such as "characterized in that the ratio between the maximum concentration.... is less than 1.35 or 1.25 etc..." do not delimit the scope of the protection to be sought and are rather to be construed as an attempt to define the invention by a **result to be achieved** (see Guidelines C-III, 4.7).

Such definitions are only allowable under the conditions elaborated in the Guidelines C-III, 4.7. In this instance, however, **such formulations are not allowable because it appears possible to define the subject-matter in more concrete terms, viz. in terms of how the effect is to be achieved by incorporating for example the type and amount of excipients used,,...**

Hence applicant's attention is drawn with the fact such formulations in 22-25 **are not recognized as a technical feature** that can confer novelty to the application, **but as a result to be achieved and therefore will be ignored for novelty assessment**.

Furthermore the present authority will assume that independent **claim 22 is made dependent on claim 1** in order to comply with the requirement of clarity according to Art.6 PCT.

Re Item V
Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2) The documents cited in the International Search Report (ISR) were numbered respectively from D1-D8; this numbering results from the citation order in the ISR and will be used for the procedure. Unless otherwise specified, the cited passages of each document in the ISR will be considered.

3) The subject-matter of present application is novel because none of the cited prior art describes a composition comprising a core of tamsulosin and a coating which contains a combination of PVAC (polyvinylacetate) and PVP (polyvinylpyrrolidone).

In particular D1 describes a tablet of tamsulosin having no food effect, but fails to mention a coating of PVAC and PVP.
D2-D6 describe a coating of PVAC and PVP which can be used for coating pellets, but fail to mention tamsulosin.
D7 is concerned with a tamsulosin pellet with an enteric coating, but fails to mention a coating of PVAC and PVP.
D8 describes a sugar sphere coated with povidone mixed with terazosin, an analogue of tamsulosin, and fails to mention a coating of PVAC and PVP.

4) However the subject-matter of present application does not involve an inventive step :

D1 (or D7 or D8), document which can be cited as the closest prior art, describes a tamsulosin tablet having no food effect, said effect seems to result from a drug matrix composed of a **pH independent release polymer** such as **HPMC or PVP** (see p.11 L.7-15, p.10 L.4-7).

The problem to be solved consists in providing an alternative composition which allows the drug release profile to be **independent** on the fasting or fed condition of a patient, that is to say the compostion has minimized food effect.

D3 (or D4-D6 or D2) teaches that Kollicoat, an aqueous dispersion composed of 27% PVAC, 2.5% PVP, provides a film-coated product which shows a drug release rate that is **independent of the pH** of the dissolution medium. As the release rate is independent of the pH, it is **implicit** that it will be also **independent of the fasting or non-fasting condition** of the patient.

Therefore, the skilled man in the art, willing to solve the problem, will use **the teaching of D3** (or D2 or D4-D6) for coating a tamsulosin core and arrive at the subject-matter of present application without being inventive.

Therefore the subject-matter of claim 1 does not involve an inventive step in view of D1 combined with D3, or even D3 taken alone or in combination with D2-D8. For the same reason, claims 2-27 are not inventive because they do not seem to contain any feature that can confer an involving an inventive step to present application.

5) In the other hand the applicant shows the reduction of the food effect for the **4**-layers beads of **example 2**, and **not for a composition** as described in claim 1, namely containing **only** a core of tamsulosin and a coating of PVAC and PVP, nor does he show the desired effect for a composition as described in claims 2-27.
It seems indeed that the reduction of the food effect is attributed to a **combination of several technical features**, which are at present time not reflected in independent claim taken alone or combined with the dependent claims.

As long as the applicant does not provide evidence that the problem is solved by a composition, wherein the ingredients or features are **all disclosed in independent claim**, inventive step will not be acknowledged because it will be considered that the problem is not solved by the subject-matter of present claims.

It appears indeed that the independent claim does not contain all the technical features essential to the invention (Art.6 PCT taken in combination with Rule 6.3(b) PCT) (see Guidelines C-III 4.4).

Re Item VII
Certain defects in the international application

6) Contrary to the requirements of Rule 5.1(a)(ii) PCT, it seems that the relevant background art disclosed in the documents D2-D6 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII
Certain observations on the international application

7) Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply and not be incorporated into the application.

8) The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the

content of the application as filed.

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT). Preferably these indications should be submitted in handwritten form on a copy of the relevant parts of the application as filed.

9) The applicant is kindly requested to take account of the above objections and **give convincing argumentations**. The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof or to restrict to a **reasonable generalisation**.